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Identifying potent and broadly-neutralizing henipaviral antigens and epitopes

Project Number 1R21Al142377-01

Contact PI/Project Leader AGUILAR-CARRENO, HECTOR

Awardee Organization **CORNELL UNIVERSITY**



Description

Abstract Text

Project Summary / Abstract The henipaviruses are a growing new genus of viruses that include the emerging and highly lethal Nipah virus (NiV) and Hendra virus (HeV). NiV and HeV cause encephalitis and pneumonia, yielding mortality rates of 40- 100% in humans. NiV is a NIAID priority pathogen listed by the World Health Organization as likely to cause future pandemics and necessitating "urgent action". Making matters worse, an additional ~20 new henipaviruses were recently discovered, raising the possibility that new henipaviruses will emerge in the human population. Unfortunately, we currently do not have approved human vaccines or therapeutic agents to protect individuals from natural outbreaks, laboratory accidents, or bioterrorism. An ideal solution would be to create potent and broadly-protective henipavirus vaccines. Although neutralizing antibodies are known to be vital for protection against henipaviral infections, a major obstacle hindering progress towards developing henipaviral vaccines is that we currently do not know what viral antigens or epitopes elicit potent and broadly-neutralizing anti- henipaviral antibodies. To fill this gap, we designed experiments that will allow us to identify such antigens and epitopes. The obtained results will aid vaccine development, future immunological studies, and the basic field of henipavirus entry. We believe it is possible to elicit broadly-neutralizing antibodies for henipaviruses because: 1) they all share structurally and functionally conserved glycoproteins required for viral entry, and 2) published and our preliminary data indicate that cross-neutralization is achievable. Further, our preliminary data indicates that distinct combinations of henipaviral antigens elicit distinct neutralizing antibody potencies and breadth of neutralization. The main goal of this R21 proposal is to understand the combination(s) of henipaviral antigens and epitopes that elicits potent and broadly-neutralizing antibody responses against henipaviruses. We are in a unique position to accomplish this goal because our laboratory has already developed a novel set of tools needed to assess and map the neutralization capabilities of antisera and monoclonal antibodies (mAbs). We will use these tools to address the following specific aims. Aim 1. Identify the optimal henipaviral protein combinations that elicit high potency and broadly-neutralizing antibody responses in a rodent model of disease. Aim 2. Identify the specific epitopes responsible for eliciting highly-potent and broadly-neutralizing antibody responses and determine where in the viral entry pathway they work. The obtained results will identify highly potent and broadly- neutralizing antibodies and their specific epitopes to best protect against future emerging henipaviral outbreaks. The knowledge gained will be useful for: vaccine development, future immunological studies, and an understanding of the role of viral glycoprotein epitopes in viral entry. In turn, such understanding will aid the development of new therapeutic strategies.

Public Health Relevance Statement

Project Narrative The emerging henipaviruses are a growing genus of viruses that include the deadly Nipah and Hendra viruses. These viruses are likely to cause future outbreaks in human populations. This study focuses on identifying viral protein elements that will allow us to formulate effective and protective vaccines against a large group of these viruses, in turn revealing targets for development of broad anti-viral therapeutic agents.

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Immunization

Infectious Diseases Orphan Drug Prevention Rare Diseases Vaccine Related

Project Terms

Address Antibodies Antibody Response Antiviral Agents Antigens **Cell fusion Binding Biological Assay Bioterrorism Cell membrane** Cells **Codon Nucleotides Data** Development **Disease Outbreaks** Disease model **Elements Encephalitis Epitopes Future G-substrate** Generations **Glycoproteins Hendra Virus** Goals Henipavirus Human **Immune Sera Immunologics** In Situ Individual Infection Knowledge Laboratories Maps **Membrane Fusion Membrane Proteins Molecular Conformation Monoclonal Antibodies National Institute of Allergy and Infectious Disease Read More**

Details

No information available for 1R21AI142377-01

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No Sub Projects information available for 1R21Al142377-01

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No Publications available for 1R21Al142377-01

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No Patents information available for 1R21AI142377-01

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

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